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USE OF MULTICHANNEL MEG IN FOCAL EPILEPSIES

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Results of magnetic field analysis in patients with pharmacoresistant focal epilepsies during the non-invasive and invasive phase of presurgical diagnostics are reported. In a first step of evaluation the accuracy of magnetic source localization was estimated by producing an experimental dipole in the depth of the mesial temporal brain region by use of depth electrodes which were applied for invasive presurgical diagnostics. The distance between the MEG-evaluated source at the tip of the electrode and its localization in the MRI was 8 mm.

Of 81 investigated patients with focal epilepsies (temporal and extratemporal) up to now the MEG-recordings of 40 patients with temporal lobe epilepsy were analysed and compared with the findings of interictal and ictal EEG-recordings during presurgical evaluation. In 74% MEG localization of epileptic activity was possible. In the group of patients with temporal lobe epilepsy and total control of seizures or marked improvement after tailored surgery the contribution of presurgical MEG for localization was investigated. In a few cases MEG-data were not available due to artefacts and external disturbances. In 72% of patients with successfully operated temporal lobe epilepsy a spatial correlation of predominant focal epileptic activity in MEG and other localization methods of presurgical evaluation as well as intraoperative ECoG was found. In some cases interictal and ictal MEG analysis was performed and compared to MRI, SPECT, PET and invasive recordings.

EEG mainly gives information of interictal and ictal recordings concerning the lateralisation and regionalisation. MEG-recording (mostly interictal) can provide additional information to EEG especially concerning the intralobar correlation of predominant focal activity and brain anatomy of regions of interest (e. g. lesion or functionally important zones).

The indications of magnetic source imaging (MSI) in focal epilepsies are discussed. Additional confirmatory tests are necessary to establish the value of MEG for the diagnostic mosaic of localization of epileptogenic area, lesion and functionally important zone. In this regard MSI may serve as a non-invasive guide.

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EVOCATION OF EPILEPTIFORM ACTIVITY BY WEAK D.C. MAGNETIC FIELDS AND IRON BIOMINERALIZATION IN THE HUMAN BRAIN

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As part of the diagnostic procedure for drug-resistent epileptic patients, electrodes are inserted into the brain via the foramen ovale (FO) and the electroencephalogram (EEG) activity recorded by these electrodes is monitored during seizures (Wieser, 1991). This procedure provides an excellent and unusual opportunity to test the sensitivity of the human brain to magnetic fields. The recent discovery of magnetite in human brain tissue (Kirschvink et al., 1992) highlights the importance of understanding how humans respond to magnetic fields.

In order to test for direct responses from the human brain to weak magnetic fields, epileptic patients with FO electrodes inserted were subjected to D.C. fields produced by a pair of coaxial coils mounted on a frame. The field generated by the coils was on the order of 0.4 mT to a maximum strength of 1.8 mT at the center of the coils. The field varied by as much as 10% to 20%, though the coils were centered over the hippocampus. During the monitoring of EEG activity D.C. magnetic fields of varying strength were applied.

Application of the D.C. magnetic fields evoked epileptiform activity in two patients whom we studied. Single or multiple events were recorded by the EEG within 10 seconds of the application of the field. Activity was also induced upon removal of the field in many cases.

In order to distinguish random epileptiform activity from that induced by the magnetic fields, 10 second intervals both before and after application of the magnetic field were examined on the EEG recordings. A peak to peak level associated with anomalous epileptiform activity was chosen in order to isolate individual anomalous events. If the occurrence of epileptiform events was random, it would be expected that the number of events occurring before application of the field would be roughly the same as the number occurring afterwards.

Examinations of the EEG recordings reveal that the first patient exhibited epileptiform activity only twice during the 10 seconds prior to application of the fields. Fields of varying strength were applied 12 times to this patient. Epileptiform activity was seen nine of 12 times within the 10 second intervals following application of D.C. magnetic fields. In most of the nine cases, several anomalous events were recorded during the interval following application of the field.

The activity was recorded on EEG channels which indicate its origin is the hippocampus. This anomalous activity involves spikes which are the most typical example of epileptiform activity. A subsequent amygdalo-hippocampectomy eliminated the epileptic seizures in this patient.

A second patient with FO electrodes was exposed to D.C. magnetic fields 17 times during the course of the experiment. Epileptiform activity was observed on the EEG recordings 11 times in the 10 second intervals following application of the fields. Again, in most cases, multiple events were recorded within this interval. There was no epileptiform activity recorded during any of the 10 second intervals prior to field application. In addition, a field of 1 mT was applied for 1.5 minutes. After a period of 30 to 40 seconds, strong, prolonged epileptiform activity was observed. This activity lasted nearly one minute. These data are being analyzed at present. Again, with this patient, the epileptiform activity appeared to originate from the hippocampus, though smaller events were seen on other EEG channels. An amygdalo-hippocampectomy was performed on this patient as well and has eliminated almost all of the epileptic seizures.

In both patients, epileptiform activity was most clearly evident in the 10 second intervals following the application of weak D.C. magnetic fields (9 responses in 12 field applications & 11 responses in 17 field applications). Within the 10 second intervals examined prior to application of the fields, there is almost no epileptiform activity (2/12 and 0/17). It therefore appears that the magnetic fields have, indeed, induced epileptiform activity in these patients.

In two other patients with FO electrodes inserted who were studied, epileptiform activity monitored by EEG occurred frequently throughout the duration of the experiment both before and after exposure to the magnetic fields. For these two patients the high level of background activity and the frequent occurrence of epileptiform events made it impossible to determine which events occurred as a result of exposure to magnetic fields and which did not.

In addition, this experiment was repeated on a non-epileptic subject with no FO electrodes inserted (electrodes were attached to the scalp only). EEG recordings showed no signs of anomalous activity when the subject was exposed to D.C. fields of the same magnitude as the other patients (0.4 mT to 1.8 mT). These results then, do not reveal whether the normal human brain is sensitive to magnetic fields of this strength. Since FO electrodes are only implanted in drug-resistant epileptic patients for diagnostic purposes, it is unlikely that results of the type documented in this study will emerge for the normal brain.

This study was, in part, prompted by the recent discovery of magnetite in human brain tissue. Investigation of tissue samples from the hippocampus of both a deceased non-epileptic and a deceased epileptic subject revealed that both contain magnetic material. This material behaved - during mineral magnetic experiments - in the manner described by Kirschvink et al. (1992) for magnetite from other parts of the brain. Fine particles of opaque material, sometimes arranged in strings and sheets, were observed in thin sections stained for iron of the hippocampus tissue from the two subjects. The origin and composition of this opaque material is not yet known. The saturation remanence of the tissue samples is anisotropic and is demagnetized by slight compression of the tissue. We therefore suspect the presence of magnetite and are investigating further.

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DIPOLE MODELS OF TEMPORAL LOBE SPIKES FROM SIMULTANEOUS MEG AND EEG

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The relationship between MEG and EEG has been the subject of much discussion. It is well accepted that MEG looses its sensitivity as cerebral sources become more radial, whereas EEG is sensitive to all source orientations. EEG potentials without MEG fields are thus understandable, but the reverse (MEG without EEG) is less well explained and has been reported only anecdotally, (Sato, 1990; Ogashiwa et al, 1991; Yotsumoto et al, 1991). Despite an unresolved debate concerning the relative utility of the two techniques, few studies have provided direct and simultaneous comparisons of MEG and EEG fields and the dipole models derived from each.

We recorded 37-channel MEG (BTi Magnes®) and 21 to 32-channel EEG simultaneously from 8 patients with presumed temporal neocortical epilepsy in order to understand better the spatio-temporal relationships between the two and to define possible clinical significance of dissociated MEG/EEG activity. Combined data were collected at the Magnetic Source Imaging Center of the VA Medical Center in Albuquerque, NM and were visually analyzed to find sharp, epileptiform MEG fields and EEG potentials that had and did not have a temporal association. We performed source analysis on both types of data, using instantaneous single and spatio-temporal multiple dipole modeling.

Epileptiform EEG potentials without MEG had simple fields and stable, radial dipole models. Spikes with associated MEG were more complex spatially and temporally. MEG spikes could lead, lag, or be synchronous with the EEG potential, and this often varied from spike to spike. Presumably this variability depended upon the activation sequence of adjacent cortical regions with different orientations. Two-dipole models of the EEG with orientation constraints (tangential/radial) often predicted MEG field orientation and timing. Conversely, MEG field characteristics could be used to help build a constrained multiple dipole model of the EEG and to resolve ambiguities in the case of more complex spike sources. MEG data revealed subtle differences in the character of tangential source components that were lost in the EEG, which was dominated by radial sources. Similarly, most patients had a greater differences in dipole orientation as well as location. Epileptiform MEG fields were also observed that had no recognizable EEG equivalent. Dipole models of these fields localized to temporal neocortical areas that were anatomically and clinically reasonable.

MEG data concerning the character of spike sources is clearly not redundant of that obtained by EEG. It appears from our data that MEG may offer a greater sensitivity to the spatio-temporal details of source configuration. Any weakness derived from radial source insensitivity can be overcome by adding complimentary EEG data. Recording spontaneous MEG for spike analysis should not be completely dependent upon EEG triggering, however, since some MEG spikes have no distinct EEG counterpart. Although ultimate confirmation of the clinical usefulness of source analysis must await intracranial EEG validation and the outcome of resective surgery, which are scheduled for all patients studied, our results suggest that MEG can have a unique role in the evaluation of partial epilepsy. The greatest benefit may come to those with neocortical epilepsy, since these syndromes are not well defined by current surface EEG and imaging techniques. Clearly, it is necessary to continue comparative analyses of simultaneously-recorded MEG and EEG in order to optimize source analysis for clinical purposes.

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LOCALIZATION OF FOCAL EPILEPTIC ACTIVITY WITH A SIMULTANEOUS EEG AND MEG MODEL

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Successful localization of focal ictal and interictal epileptiform activity by means of MEG measurements has been reported by several laboratories (Ricci et al., 1985; Sutherling et al., 1985; Rose et al. 1987; Stefan et al., 1992). On the other hand, EEG models have been rarely used to identify the 3–D position of foci; recently, Nakasato et al. 1992) compared MEG and EEG based localizations in two patients and obtained significant differences between the two methods in one of the patients. So far, there appear to be few attempts to *combine* simultaneous EEG and MEG measurements into a single model ("simultaneous MEG and EEG model", SMEM) for the localization of epileptiform activity; in view of the disjunctive sets of information provided by MEG and EEG, such a combination might improve functional localizations.

Computer simulations of single dipolar sources by Stok (1987) and in our laboratory suggest that SMEM should produce better results than the averaging of separately fitted MEG and EEG models (AMEM). We have confirmed these predictions by investigating a physical model consisting of a current dipole positioned within a glass sphere (inner radius 9.6 cm) filled with a 0.9% NaCl solution. The magnetic field outside the sphere was measured using our DORNIER MEG–system (two cryostats, each housing 14 magnetometers based on DC–SQUIDs developed at the University of Jena) in a magnetically shielded room. The sphere's coordinates were determined from the magnetic fields generated by marker coils attached to the outer surface along the equator. The electric field at the liquid–glass boundary was sampled by electrodes glued to the sphere's inner surface in analogy to the 10–20–system. The MEG and EEG data were given equal weight by transforming their amplitudes into the range [0,1], and the combined set of data then was fitted to a spherical magneto–electric model using standard non–linear approximation techniques. With regard to the the tangential (Θ, ϕ) coordinates (mean error 3 mm), the accuracy of dipole localization obtained from this procedure was similar to that of the AMEM approach, whereas for the radial (depth) direction SMEM was clearly better (mean error 2 mm) than AMEM (mean error 5 mm).

In view of the encouraging results of these physical and computational simulations, we have reviewed simultaneous measurements of MEG and EEG obtained from more than 30 epileptic patients in our laboratory during a period of 18 months. For these measurements the two cryostats of the MEG system were positioned symmetrically with respect to the left and right hemispheres over areas of potential interest. Patients were equipped with electrodes at all positions of the 10–20–system and with markers attached to landmarks (nasion, preauricular points) defining a head coordinate system. The markers and the electrodes could be magnetically localized (Becker et al., 1992) thus allowing to project the positions of the electrodes and of the pick up coils upon MRI scans of the patients' heads. In the example shown in Fig. 1, a four layer spherical model was fitted to the geometry of the posterior head as obtained from the MRI, assuming conductivities of 0.33, 1., 0.0042, and 0.33 S/m for brain tissue, CSF, bone and scalp, respectively. The SMEM localization of a single equivalent current dipole (SECD) obtained in this example (marked by open circle) is compatible with the patient's ictal focus in the left posterior temporo–basal region suggested by epicortical strip recordings. It is clearly more appropriate than a pure EEG model (diamond), but there was no noticeable improvement over the purely magnetic approach (triangle); our experience so far indicates that this is typical for many practical cases.

There are several obvious reasons for this failure of SMEM in our patients to live up to its theoretical promises:

(i) Most patients had deep sources with correspondingly small ratios of spike to background activity which could not be improved by linear (e.g. Abraham–Fuchs et al., 1992) or non–linear filtering techniques and which cause any model to make inherently unstable predictions

(ii) To our experience, complementary dipolar MEG and EEG fields are rare exceptions when both hemispheres are considered at the same time. Even if, at some instant, the magnetic field is fairly dipolar, its electric counterpart is generally not and calls for multipole instead of SECD fits. On the other hand, given the typical ratios of spike–to–background amplitudes, multipole fits can be expected to be extremely unstable.

(iii) The 19 electrodes of the 10–20–system collect information from all over the head while the spherical layers representation used in our models is clearly inappropriate to describe the head as a whole.

In summary, an improvement of spike localization by usage of SMEM as compared to AMEM or purely magnetic models can be expected only if these models take into account the real head geometry and if spikes occur with sufficient signal–to–noise ratio – a condition that generally will hold only for more superficial sources than those typical of the population of patients we have investigated so far.

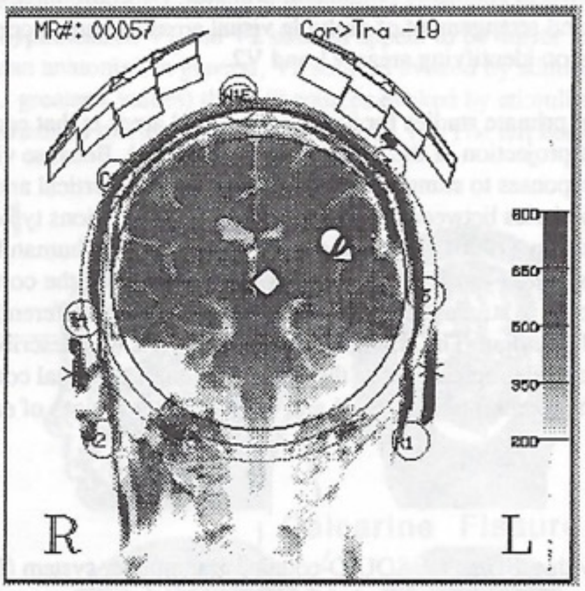

Fig. 1

MRI (coronal slice) of a patient with complex partial epilepsy (23 y, female). Projected onto the MRI are shown the magnetically determined positions of (i) the square shaped pickup coils, (ii) the preauricular markers (stars), (iii) electrodes A1,T3, C3, Cz, C4, T4, A2. Fit of head geometry by spherical layers and location of equivalent current dipoles

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MEG STUDIES OF HUMAN VISION: IDENTIFICATION OF AREAS V1 AND V2

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INTRODUCTION

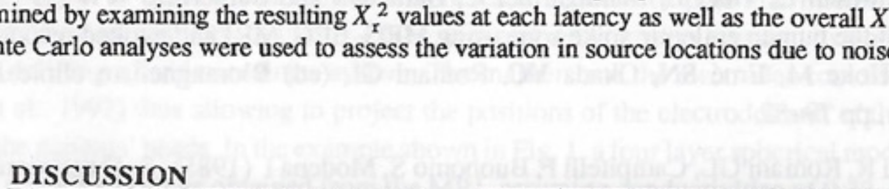
A primary goal of noninvasive studies of human vision is to identify and characterize multiple visual areas in the human brain analogous to those identified in studies of nonhuman primates. By combining MEG measurements with MRIs, we hope to determine the location and arrangement of multiple visual areas in human cortex and to probe their functional significance. This paper focuses on identifying areas V1 and V2.

One criterion used in nonhuman primate studies for identifying visual areas is that each area must have some retinotopic organization (i.e., point to point projection of the visual field onto cortex). Because visual areas are retinotopically organized, analyses of neural responses to stimuli placed along or near the vertical and horizontal meridians in the visual field can aid in defining the boundaries between visual areas since these locations typically project to the edges of cortical areas. Recently, Clarke and Miklossy (1990) identified several visual areas in human brains, consistent with maps obtained in nonhuman primate studies (Van Essen et al., 1982), by examining the cortical distribution of visual callosal afferents in stained slices. As noted in studies of nonhuman primates, callosal afferents preferentially terminate in regions representing the vertical meridian. The arrangement of V1 and V2 was described as follows: 1) V2 is horseshoe-shaped around V1 with the upper field represented in the lower portion of occipital cortex (i.e., below the calcarine fissure) and vice versa; and 2) the representations in V1 and V2 are mirror images of each other.

METHODS

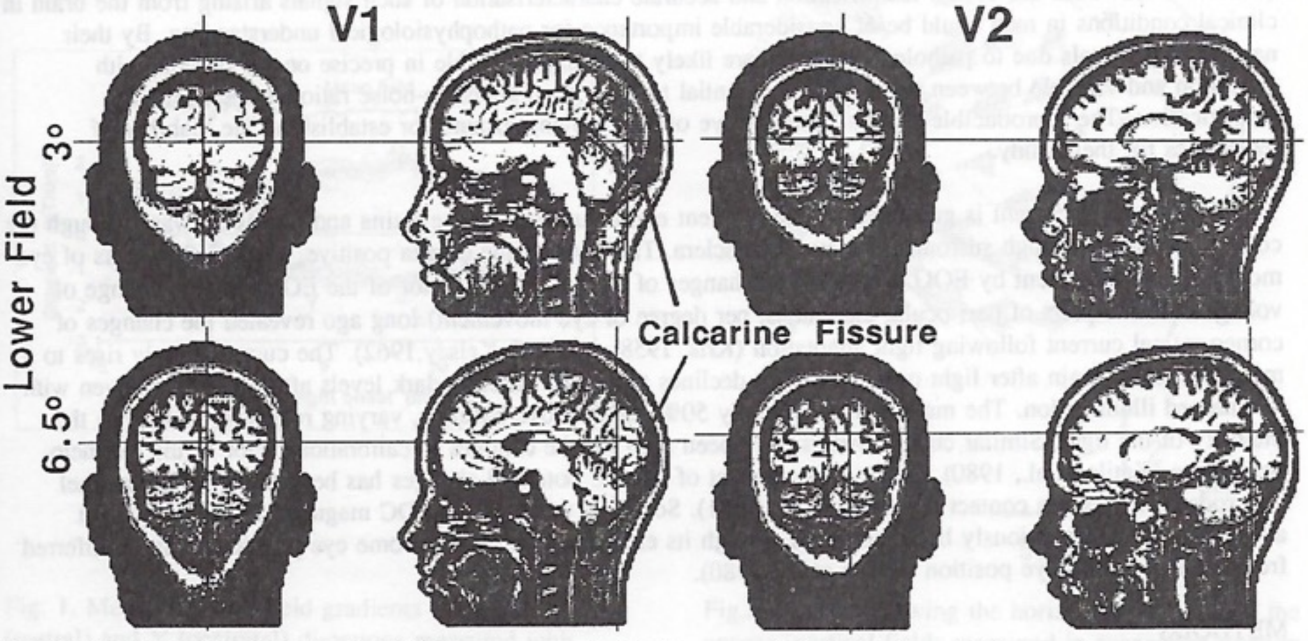
Magnetic fields were recorded with a 7-channel, SQUID-coupled gradiometer system (BTi) while subjects viewed computer-generated visual displays. Data were recorded from 10 subjects during one of two experimental protocols: a) circular sinsusoids (Targets), ranging in size from .4-1° (adjusted for cortical magnification), were presented randomly and sequentially to 7 different locations in the lower right quadrant of the visual field; and b) 2-dimensional, difference of gaussians (DOGs) were presented at 3° and 12° in the upper and lower right field. Stimulus duration was 266 ms and the rate of presentation was randomized with an average rate of 1 Hz. During a given experiment, the 7-sensor array was moved to several locations over the surface of the head and the conditions were repeated for each position of the array. Field amplitudes were measured from the prestimulus baseline at 5 msec intervals. Iso-amplitude maps were constructed for each latency by interpolation across all sensor locations. A multi-dipole, spatial-temporal model, using a simplex search, was applied to various intervals of time (e.g., 80-120 ms, 80-150 ms, 80-165 ms, etc.). This model restricts the location of the dipoles to be constant throughout the measurement interval, but allows the moment intensities and orientations to vary. Initial starting parameters were determined from a sampling of instantaneous fits and model adequacy was determined by examining the resulting X_r^2 values at each latency as well as the overall X_r^2 (Supek and Aine, in press). Monte Carlo analyses were used to assess the variation in source locations due to noise (Medvick et al., 1989).

RESULTS AND DISCUSSION

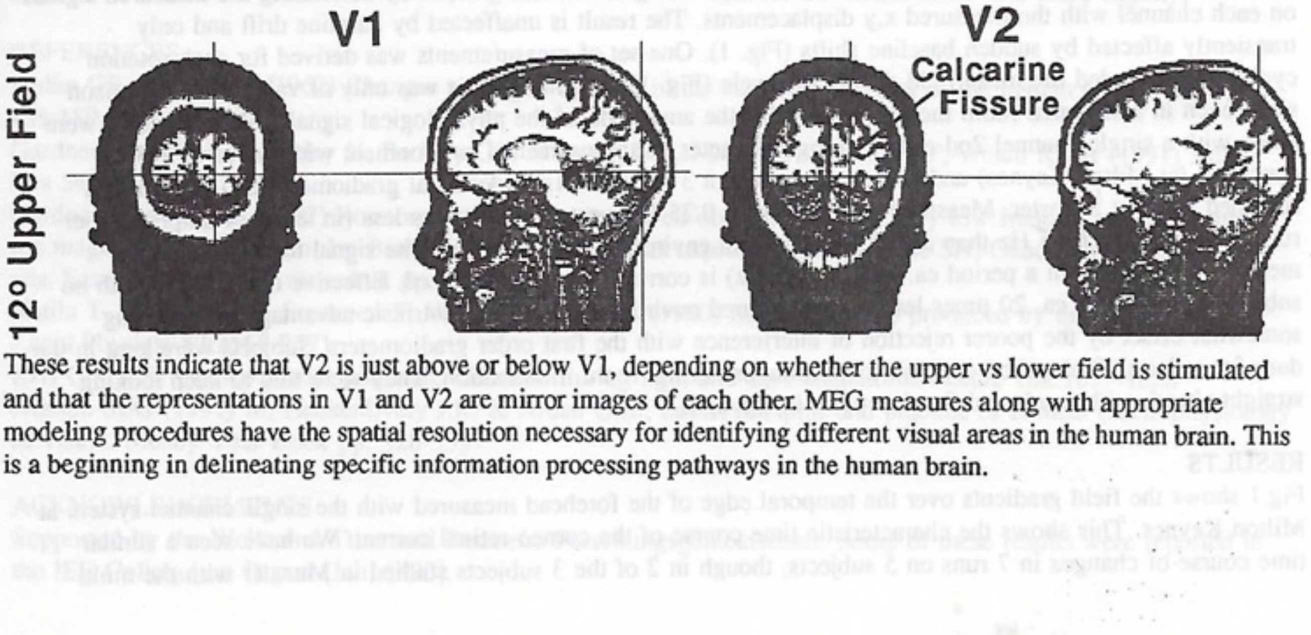


Three to five sources have been identified for each of the subjects during the initial 80-165 ms interval poststimulus. Variations in source location for 100 Monte Carlo solutions are illustrated above as contour plots in register with 3-D MRI data. Five regions were active in response to a Target presented 4° below the horizontal meridian and 3° to the right of the vertical meridian: V1, V2, left occipital-temporal, medial occipital-parietal, and an ipsilateral right hemisphere source. Four sources are shown in the reconstructed image in the left column and a 5th source, striate or V1, is shown in the right column. The left hemisphere is displayed on the left side in this figure.

The V1 and V2 sources modeled and displayed below (denoted by cross-hairs) are consistent with the Clarke and Miklossy results. The V1 source (first two columns) became progressively deeper when the stimulus was placed more peripherally (3° vs 6.5°) and the V2 source (last two columns) was lateral and dorsal of the V1 source. The V2 source was closest to the V1 source when the stimulus was located near the vertical meridian (first row: 3°) and the V2 source was most distant from the V1 source when the stimulus was located near the horizontal meridian (second row: 6.5°). Therefore, the retinotopy of the hypothesized V1 and V2 sources appear to be mirror images of each other, consistent with the primate results and human anatomy. In general, V2 sources evoked by stimuli near the horizontal meridian (e.g, 6.5°) were more dorsal (i.e., greater z values) than V2 sources evoked by stimuli near the vertical meridian (e.g., 3°) since the representation of the horizontal meridian in V2 borders area V3. The left hemisphere is displayed on the right side in these figures.



Results from another subject, when DOGs were presented to the upper right field, show similar trends and add to the above results by showing: 1) the V1 source was on the lower bank of the calcarine fissure for upper field stimuli; and 2) the V2 source was inferior and lateral of V1 for stimuli presented in the upper field, again consistent with the anatomy.



These results indicate that V2 is just above or below V1, depending on whether the upper vs lower field is stimulated and that the representations in V1 and V2 are mirror images of each other. MEG measures along with appropriate modeling procedures have the spatial resolution necessary for identifying different visual areas in the human brain. This is a beginning in delineating specific information processing pathways in the human brain.

BENIGN FOCAL EPILEPSY OF CHILDHOOD -
A COMBINED NEUROELECTRIC AND NEUROMAGNETIC STUDY

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INTRODUCTION

Benign focal epilepsy of childhood (BFEC) is one of the most frequent epileptic syndromes in patients less than 15 years old. Clinically, the syndrome is characterized by facial motor seizures sometimes preceded by a somatosensory aura and by generalized tonic clonic seizures during sleep or on awakening. The prognosis is excellent and most patients become seizure-free after the age of 15 years (Lüders et al. 1987).

The interictal spike complex in BFEC has been studied extensively. It has been found that the spikes show very characteristic waveforms and distributions and are significantly activated by sleep. Typically, the spikes show a stereotypic morphology, are located in the centrotemporal region, and - in contrast to the spikes in temporal lobe epilepsy - often exhibit a dipolar potential distribution. Recent studies have suggested that some of the spikes in BFEC are generated by multiple, simultaneously active neuronal sources (Gregory and Wong 1984).

The aim of the present study was to investigate interictal spikes in this epileptic syndrome by simultaneous neuromagnetic and neuroelectric measurements and to exploit the complementary and confirmatory information provided by the two techniques. We applied multiple dipole modeling to study the spatiotemporal structure of the underlying neuronal sources (Baumgartner et al. 1989; Scherg 1990). Furthermore, we related the results of source localization to those obtained from modeling of somatosensory evoked responses and thus could compare neuronal activation under physiologic and epileptic conditions.

METHODS

We measured spikes and somatosensory evoked responses (SERs) in 12 patients with benign focal epilepsy of childhood both on magnetoencephalography (MEG) and on scalp-EEG. Neuromagnetic recordings were performed with a 7 channel magnetometer with dc-SQUIDs (second derivative gradiometer; coil diameter 15 mm; coil baseline 40 mm; Biomagnetic Technologies Inc., San Diego, CA) in a large electromagnetically shielded room (Vacuumschmelze GMBH, Hanau, Germany). Scalp-EEG was measured from 48 gold disc electrodes placed according to the International 10-10-System and was amplified with high quality amplifiers (Grass 12A5 amplifiers, Grass Instruments Company, Quincy, MA). MEG and scalp-EEG measurements were performed simultaneously.

SERs were recorded in response to shock stimulation of the median nerve at the wrist. Stimuli were delivered by a Grass S88 stimulator (Grass Instrument Company, Quincy, MA) and consisted of monophasic, constant current 0.3 msec pulses.

Finally, we applied single and multiple dipole modeling to study the number, the three-dimensional intracerebral location, the orientation and the time activity of the sources generating the epileptic spike complex and compared them to those underlying the SERs.

RESULTS

We found that a variable number of sources was underlying the epileptic spike complex in BFEC. Whereas some spikes were generated by a single generator (Fig 1.) other spikes were generated by multiple, simultaneously active brain regions overlapping both in space and time. Multiple dipole modeling could separate the potential and field contributions of the various sources. Concerning source location, the results of scalp-EEG and MEG showed good agreement. Finally, the sources underlying SEPs and SEFs were used as functional landmarks of sensorimotor cortex and related to those underlying the epileptic spike complex.

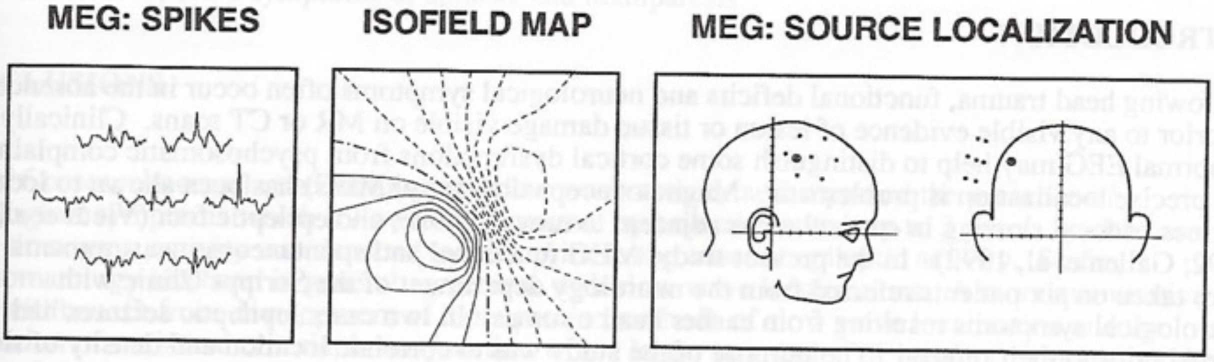

Fig. 1. Spike recorded on MEG. Original traces obtained with the 7-channel magnetometer (left). Isofield map (middle). MEG source localization obtained at maximum spike amplitude (MEG coil locations: small dots, source location: large dot; right).

DISCUSSION

Wee conclude that some of the spikes in benign focal epilepsy of childhood are generated by multiple, simultaneously active neuronal populations generating fields which overlap both in space and time. Multiple dipole modeling was useful to study the number, the potential and field contributions, the three-dimensional, intracerebral location, the orientation and the time activities of the neuronal sources underlying the epileptic spike complex. This approach enabled us to study the functional organization of the epileptogenic regions. The source locations underlying the somatosensory evoked responses served as useful functional landmarks in order to establish a spatial relationship of the epileptogenic zone to sensorimotor cortex. Finally, scalp-EEG and MEG yielded both complementary and confirmatory information and thus helped to better define the spatiotemporal structure of the epileptic spike complex.

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OBJECTIVE TESTING OF HARMONIC PROCESSING CAPABILITIES BY MEG

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INTRODUCTION

The goal of the present study was to investigate a certain aspect of auditory processing in musically experienced subjects, that is processing of harmony. Although there are studies performed with EEG (Altenmüller, 1986) or dichotic listening (Sidtis, 1980), this question has not been approached by use of MEG yet. Judgement of harmonic relationships between chords or tones (which are actually chords since natural tones are comprised of many harmonics) rely probably on experienced knowledge. Strong cultural influences can be expected and are manifest in considerable variability concerning native musical scales and native senses of harmony. We tested subjects exposed to classical european music from birth. All played at least one western instrument. By use of the P300m we designed an experiment which should allow for testing the internalisation of harmonic meaning of a certain tone in a given context. P300 has already been successfully used for investigating processing of melodies (Verleger, 1990). In our experiment the subject had to recognize a presented tone as not belonging to the musical context heard before for generation of a P300m. As such it served as an indicator for successful harmonic processing according to the rules of western musical harmony.

MATERIALS AND METHODS

20 musically experienced subjects (each performing an instrument) were presented the first 3 chords of an ordinary cadenza: I, IV, V. Instead of the fourth chord we presented a target tone. That was either a harmonically fitting tone (75% of the cases, consisting either of the fundamental of the tonic, the third, or the sixth) or a harmonically non-fitting tone (25% of the cases, being the minor second to the fundamental of the tonic). The non-fitting target had to be counted. Every target tone occured with equal probability in all 4 cases (tonic, third, sixth, minor second) and in total we used 11 different pitches (completely randomised) preceded by the corresponding chords. All stimuli were presented to both ears. 7-21 measurement positions over the right parietotemporal area were used to record the magnetic fields associated with processing of the target tones. The indicator used for observing tone processing was the magnetical equivalent of the P300 (P300m). By use of the same tones for the fitting as well as for the non-fitting targets we made sure that a differentiation could only be performed by reference to the harmonic context heard before. In addition we tried to minimize memory effects regarding the test stimulus by using tones instead of chords.

RESULTS

The main question of this study was, whether it would be possible to find neurophysiological correlates of harmonic processing in the human brain. If the subject was able to differentiate whether the target tone fits or fits not to the preceding harmonic context, a distinct magnetic wave starting around 300 ms post stimulus onset was expected (P300m) to occur in the non-fitting condition (minor second). Note, that a differentiation of the "harmonic load" of the target tone could only be performed as a consequence of the preceding chords since *every* target tone was preceded by harmonically fitting as well as non fitting contexts. In addition we used three different fitting contexts so that the probability for a change of intervals between the last chord and the target tone could not be used as a cue. Results show, that subjects who are able to perform well, indeed show such a P300m (see Fig.1) whose extrema were found over the right temporoparietal junction. The localisation of the process and corresponding EEG data will be discussed with respect to P300m reports of other groups (e.g. Rogers, 1992).

CONCLUSION

This study provides a basic access to the evaluation of a certain type of man's cognitive abilities, that is harmonic processing. Further development therefore, could increase the battery of objective tests available for musical ability. In addition, cross-cultural investigations should help to further evaluate the nature of the underlying processes and the amount of biological and environmental influences on them.

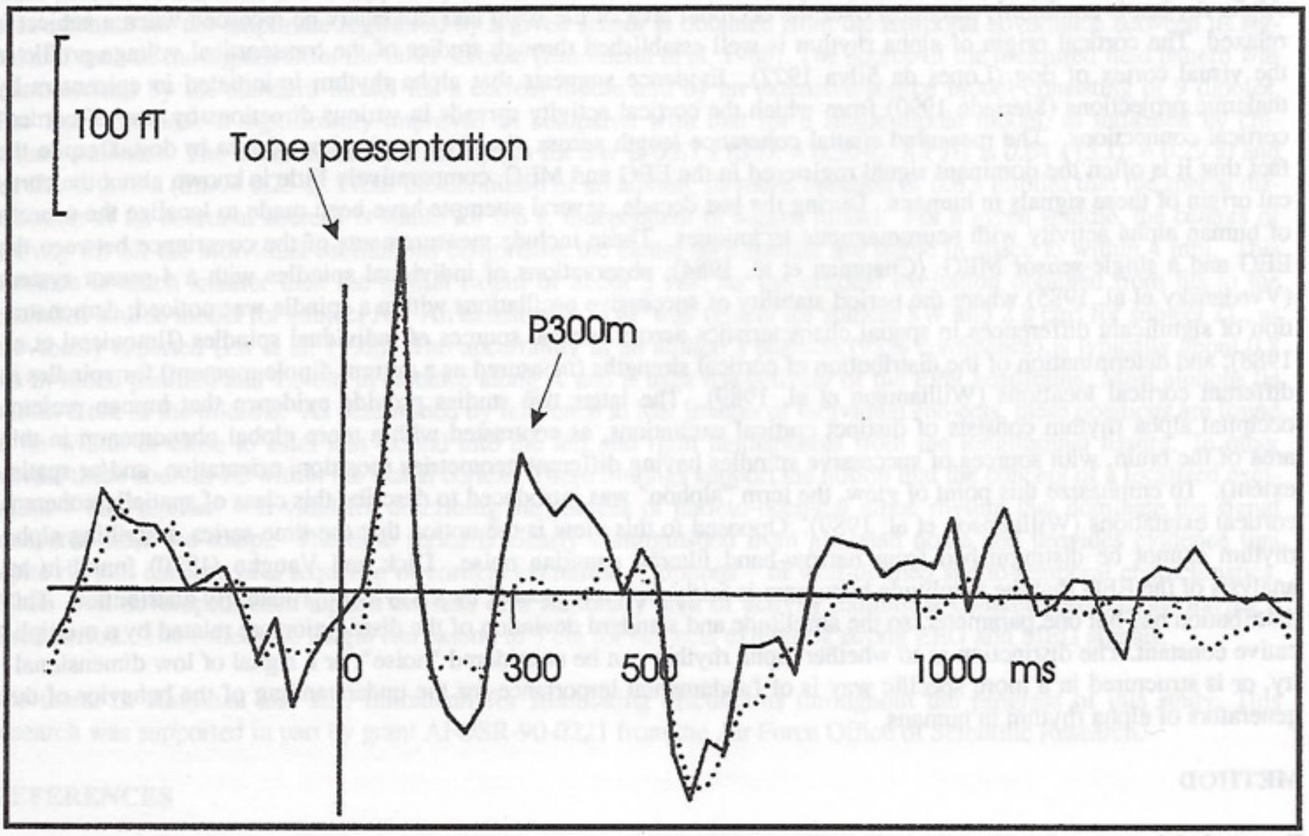

Fig. 1: Averages as recorded at one channel. The solid line shows the magnetic field course following the harmonically fitting tone. The dotted line shows the average of the non fitting tones. Note the P300m starting about 300ms after tone presentation.

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EVALUATION OF MUSIC-BASED INITIAL SOURCE MODELING ASSUMPTIONS FOR SPATIO-TEMPORAL FITTING OF SIMULATED MULTI-SOURCE NEUROMAGNETIC DATA

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INTRODUCTION

Inferences regarding source locations, orientations, and the time courses of sources active during an interval of interest of an evoked neuromagnetic response can be obtained either by modeling a series of instantaneous field distributions or by spatio-temporal modeling of the selected spatio-temporal data matrix. The underlaying assumption in both cases, whether implicit or explicit, is that a small number of dipoles (moving or fixed locations) with varying time-courses can account for the data. To estimate best-fitting parameters by nonlinear minimization, specific source modeling assumptions are required, e.g., the initial starting parameters must be provided by the investigator. However, determining the number of active sources and their locations and orientations a priori presents a challenging problem. A MUSIC-based algorithm (Mosher et al., 1992) was recently applied to MEG data with the goal of overcoming these difficulties. By 1-dipole scanning over a selected 3-D grid of possible source locations, MUSIC provides suboptimal estimate of the actual source locations which are expected to represent good starting points for spatio-temporal fitting. As a result of spatio-temporal minimization, improved location parameters are available as well as the estimates of the time courses. While the investigator is still expected to make decisions about signal subspace boundaries by performing singular value decomposition (SVD) of the spatio-temporal data matrix, location parameter estimates are now data based and may be derived quickly by scanning a volume of interest.

The goals of this simulation study were to evaluate: 1) the ability and limitations of MUSIC based approach for providing good initial estimates of actual multi-source locations for spatio-temporal modeling and 2) the effects of spatial source configurations, temporal correlations and noise on MUSIC-based solutions.

SPATIO-TEMPORAL SIMULATIONS

Spatio-temporal neuromagnetic data were calculated for dipolar sources of fixed locations and orientations, embedded in a homogeneous spherical conductor (R=10cm), with either synchronous or asynchronous time courses. A series of 2-dipole spatio-temporal data were generated by varying source location and orientation parameters, degree of temporal correlation, and noise level . We also simulated 3-dipole data where 2 of the sources of different strengths were activated synchronously followed by asynchronous activation of a third source. This particular spatial configuration and temporal sequence of activation are typical of those encountered in the analysis of empirical visual data (Aine et al., 1993). The number of sources and their location parameters identified by MUSIC were used as starting points for spatio-temporal fitting where the time courses were estimated by linear least squares estimation (e.g., initial time courses). By iterative minimization, using a simplex search, location parameters were improved and the final time courses were estimated. Goodness-of-fit of the model to the data was evaluated by χ_r^2 values (Supek and Aine, 1993) for both the overall fit to the data as well as at each instant in time. Additional starting points for spatio-temporal modeling were provided by fitting instantaneous field distributions at selected time slices.

RESULTS AND DISCUSSION

The simulations demonstrated that the correct number of underlaying sources and accurate source location estimates can be obtained by MUSIC scanning only in cases where the sources were separated enough and asynchronously activated (Fig. 1A). The degree of temporal decorrelation was found to aid in source resolution as well as source orientations (Fig. 1B and C, respectively). Maximum value(s) of the MUSIC scanning metric were often not indicative of underlying source multiplicity. Due to the above limits in source resolution of MUSIC scanning and its inability to resolve synchronously active sources independent of their separation and orientation, MUSIC solutions tended to provide a smaller rather than the accurate number of sources; therefore, MUSIC solutions should be considered only as one set of the starting points for spatio-temporal modeling. As a result of such undermodeling large errors were introduced in source locations and in the estimated time courses. For example, actual uni-modal source activity was estimated as multi-modal pattern. Our simulations indicated that exhaustive search across model orders and starting points may be avoided by determining the number of dipoles and location parameter estimates by fitting instantaneous field distributions at selected instants in time, provided a small number of fixed dipoles with changing time courses can explain the data. However, even for the correct model order, there is a great sensitivity to starting conditions, i.e., small variations in the starting location points around actual location parameter values may result in inaccurate

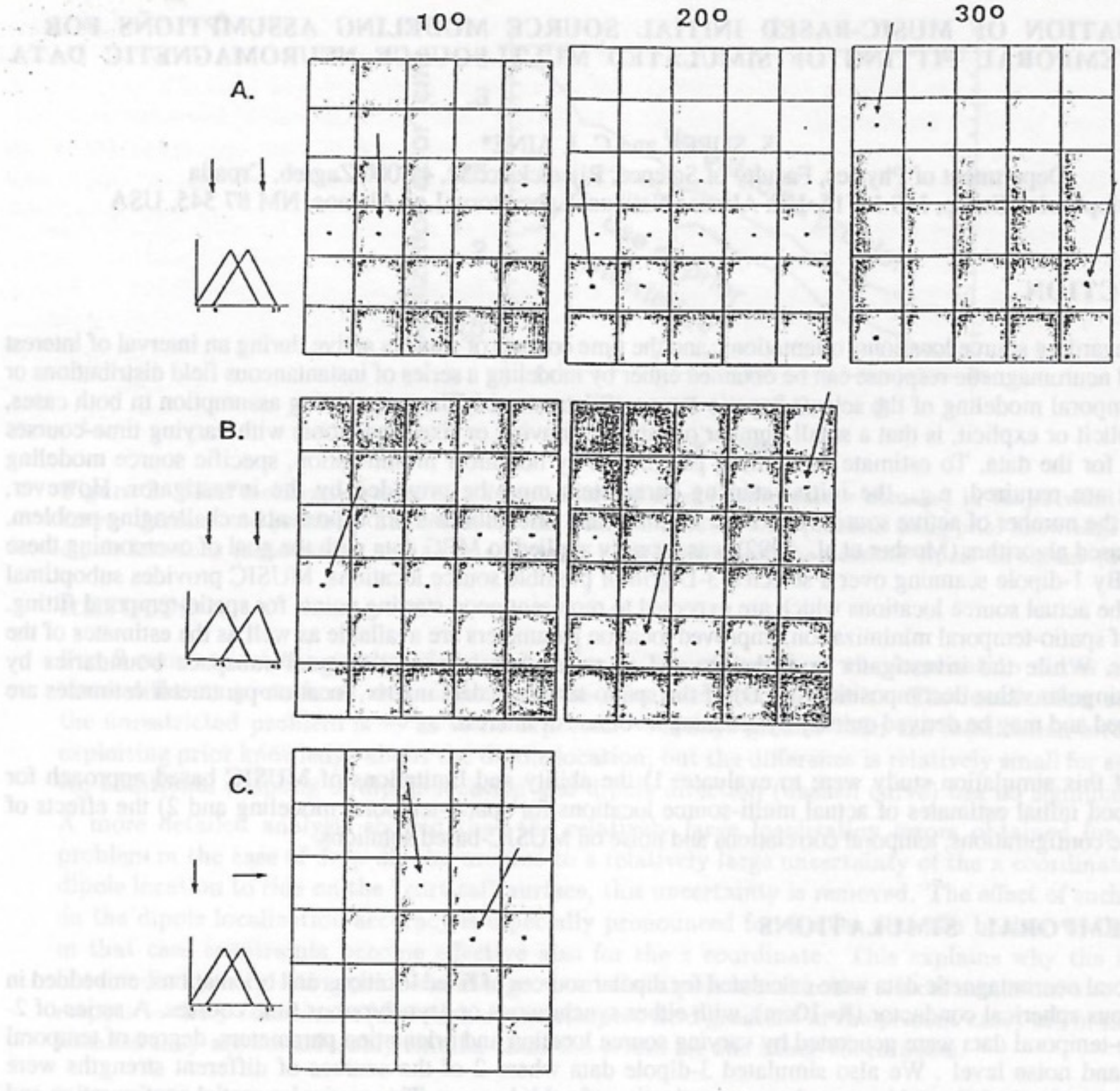

Fig. 1: MUSIC results for a series of noisy (SD=20 fT) 2-dipole spatio-temporal data: asynchronous activity. Metric peaks, corresponding to estimated source locations, are indicated by arrows.

estimates of time courses. In addition, for asynchronous source activation, non-zero moment values were obtained at each instant in time over a chosen time interval for all sources. These characteristics of the time courses estimated by spatio-temporal modeling make it difficult to infer the onset of activity in different brain regions and their duration in empirical studies, information which is important for tracking sensory and cognitive streams of cortical processing.

Fig. 1: MUSIC results for a series of noisy (SD=20 fT) 2-dipole spatio-temporal data: asynchronous activity. Metric peaks, corresponding to estimated source locations, are indicated by arrows.

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